

NCRR Reporter

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CRITICAL RESOURCES FOR RESEARCH



U.S. Department
of Health and
Human Services



Building Critical Resources for Health and Economic Gain



Advancing science to improve health and stimulate the economy

The American Recovery and Reinvestment Act (ARRA) of 2009 provides \$10.4 billion to NIH for two years. The funds are boosting existing health research programs and creating new ones, speeding advances in science and medicine.

They also are breathing new life into our economy. New grants create or preserve jobs for lab technicians, postdoctoral fellows, research assistants, students — even architects and construction workers. The resulting research may lead to new preventions, treatments and cures for diseases. Industry also can translate findings into new medical devices or instruments, which in turn lead to jobs in manufacturing and marketing.

NCRR is administering more than \$1.6 billion in ARRA grants in several areas. As referenced in the ARRA legislation, NCRR received \$1 billion for construction, repair and renovation of research facilities and \$300 million for shared instrumentation and other research equipment. Additionally, NIH allocated \$310 million to NCRR in support of other biomedical research priorities.

We expect that the positive impact of this support for institutions and researchers — as well as for other sectors of the economy — will be extraordinary, but it will take some time before we can gauge its full extent. The cover story in this issue of the *NCRR Reporter*, which highlights several institutions that received NCRR's construction and instrumentation grants in the past, provides a glimpse of what the future may hold thanks to ARRA funding.

Previous funding at the University of Puerto Rico, for example, resulted in construction of the first building in the commonwealth dedicated solely to research. At the University of California, Los Angeles, School of Medicine, construction of a new facility helped fill a gap in the field of neuroimaging. The New York Structural Biology Center in New York City, a facility essential to the work of structural biologists in the region, leveraged NCRR funding to expand its size and capabilities.

Research facilities would be of little value to scientists without the advanced instruments, lab equipment, high-powered computers and other resources they house. NCRR-funded high-end and shared instrumentation grants provide thousands of researchers with the cutting-edge equipment they need to peer into the inner workings of molecules, cells, tissues and whole organisms to unravel disease processes.

Today as in the past, NCRR grants can help create jobs, stimulate the economy and, most importantly, advance scientific discoveries to improve human health.

Barbara Alving, M.D.

Barbara Alving, M.D.
Director, NCRR

3 CTSAs in Focus

CRITICAL RESOURCES

4 Building Critical Resources for Health and Economic Gain

Funding state-of-the-art buildings and equipment to enable research advances and create new jobs.

ESSENTIAL TRAINING

9 Filling the Vital Need for Veterinary Researchers

RESEARCH TO REALITY

11 Examining the Brain's Fine Structure

FUNDING MATTERS

13 Expanding Drug Discovery in Kansas

14 Dynamic Cells at the Maryland Science Center

15 News from NCRR

NCRR Reporter



This quarterly publication of the National Center for Research Resources fosters communication, collaboration and resource sharing in areas of current interest to scientists and the public.

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On the Cover:

Architect Nannette Rodriguez (left) and builder Mark Crudup discuss plans for a new facility at the University of Puerto Rico. Behind them is an artist's rendition of the building — the first in Puerto Rico to be designed exclusively to support research. NCRR supported the building's construction with Extramural Research Facilities Improvement grants. Professor Loyda Meléndez (right) and other university colleagues will use the new facility to conduct research in such areas as neuroscience, cancer and molecular studies.

ARTIST RENDITION COURTESY OF THE UNIVERSITY OF PUERTO RICO; PORTRAITS BY PACO MÁRQUEZ

► CTSA Progress Report



In July, NCRR released the first CTSA Progress Report — *Advancing Scientific Discoveries Nationwide to Improve Health* — which highlights the innovations, collaborations and partnerships that emerged from the CTSA consortium from 2006 through 2008.

The report illustrates how the CTSAs are enabling researchers to develop novel approaches that accelerate treatment and prevention strategies for both common and rare disorders.

To read the full report, visit www.ncrr.nih.gov/ctsa/progress_report_2009.

► Consortium Welcomes Seven New Members

In July, seven academic health centers received CTSAs, joining the University of Cincinnati as 2009 grantees. Growing to 46 CTSA institutions, the national consortium expanded to Arkansas, Florida and South Carolina. The CTSA network now includes awardees in 26 states. The program eventually will support about 60 CTSAs nationwide. The new institutions and principal investigators are:

- Medical University of South Carolina (Charleston), Kathleen Brady
- Mount Sinai School of Medicine (New York City), Hugh Sampson
- New York University School of Medicine (New York City), Bruce Neil Cronstein
- University of Arkansas for Medical Sciences (Little Rock), Curtis Lowery

- University of Florida (Gainesville), Peter Stacpoole
- University of Illinois at Chicago, Theodore Mazzone
- University of Texas Medical Branch (Galveston), Allan Brasier

Learn more about the new awardees at www.ncrr.nih.gov/ctsa2009.

► A New Look for CTSAweb.org

The consortium Web site, CTSAweb.org, now has a new look and more user-friendly navigation. User feedback guided site improvements, including more graphic elements and better content flow.



New features include:

- Streamlined navigation menus organized around specific audience needs.
- New regional consortia pages.
- Links to Strategic Goal and Key Function Committee information.
- Graphic boxes to highlight consortium news, strategic goals and featured institutions.
- A communications toolkit refocused on the needs of consortium members, including a CTSA slide set, logo and banner.
- A new media resource page for reporters, editors and others.

Explore these features on the redesigned site at CTSAweb.org.

► Web Resource Provides Drug Data for Alternate Uses

The CTSA Pharmaceutical Assets Portal, launched earlier this year, allows scientists to learn about compounds evaluated for specific diseases that might be used to treat other conditions. Kate Marusina of the University of California (UC), Davis, turned the portal concept into reality with an NCRR-funded administrative supplement. With these funds, an academic consortium of five CTSAs, led by the UC Davis Clinical and Translational Science Center (CTSC), developed the portal to give researchers access to a database of existing compounds that can be “repurposed” for use in other studies. According to UC Davis CTSC Director Lars Berglund, this new resource may accelerate the research process, allowing patients and their doctors to benefit from results sooner. Other consortium members include the University of Washington, the Oregon Health & Science University, the University of Pennsylvania and the University of Chicago. The team also partnered with industry to gather the initial data.

For more information, visit www.ctsapharmaportal.org. ■

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The Clinical and Translational Science Award (CTSA) program created a national consortium designed to transform how biomedical research is conducted across the country. Its goals are to speed the translation of laboratory discoveries into treatments for patients as well as to train a new generation of clinical researchers. The CTSA program is led by NCRR. For more information, visit CTSAweb.org.
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Building Critical Resources for Health and Economic Gain

Funding state-of-the-art buildings and equipment to enable research advances and create new jobs. **BY LAURA BONETTA**

State-of-the-art research facilities that encourage interaction and collaboration among scientists; cutting-edge instruments that enable breakthrough discoveries; powerful computers and programs that process and store massive amounts of data; highly skilled scientists, technicians and students — these are key ingredients for a thriving research environment.

Establishing this critical infrastructure not only advances science and medicine but also spurs economic growth. Investments in research create new positions for scientists and support staff, advance discoveries, and promote education in science and medicine, all of which lead to better health and a more productive workforce. Construction of research buildings requires many workers, from architects and builders to facility and technical staff. Jobs in engineering, manufacturing and sales result from the purchase of laboratory equipment and reagents.

The far-reaching economic impact of investments in research is one reason the American Recovery and Reinvestment Act (ARRA) of 2009 provides \$10.4 billion to NIH for two years. NCRR will administer more than \$1.6 billion in ARRA grants in several areas, including \$1 billion for construction, repair and renovation of research facilities; \$300 million for shared instrumentation and other equipment; and up to \$310 million in support of biomedical research priorities. (See the sidebar on page 7 for a list of grants.)

Some NCRR ARRA-funded grants already have been awarded; their impact on job creation, economic growth, and advances in science and medicine will become clear in the months and years ahead. For now, past examples from institutions that received similar grants provide a look at what the future may hold.

FACILITIES FOR THE FUTURE

In San Juan, the University of Puerto Rico, Río Piedras Campus, received Extramural Research Facilities Improvement grants (C06 construction grants) from NCRR in 2000 and 2002. The university combined these grants with commonwealth funds to begin construction of a 152,000-square-foot research facility. “It will be the first building in Puerto Rico to be designed and built exclusively to support research,” said Emma Fernández, vice president for research and technology at the University of Puerto Rico (UPR), the first public university in the commonwealth. “This building is an icon for the knowledge-based economy Puerto Rico wants to pursue.”

UPR matched each \$2 million NCRR grant, which gave the Río Piedras Campus \$8 million to start construction. The government of Puerto Rico then provided an additional \$25 million for the building, and UPR added \$35 million to reach the total construction cost of \$68 million. “It is a great example of what can be achieved with federal grants if you can leverage that money with government and university funds,” Fernández said.

“We have doubled external funding every five years, and NCRR has played a significant role in that growth.”

—EMMA FERNÁNDEZ, VICE PRESIDENT FOR RESEARCH AND TECHNOLOGY AT
THE UNIVERSITY OF PUERTO RICO

The first phase of construction, to be completed in December 2009, will produce 12 laboratories for research in neuroscience, cancer and molecular studies. “To support that research, we are focusing on state-of-the-art technologies, such as proteomics, nanotechnology and molecular genetics,” Fernández explained.

Architects used the latest concepts in laboratory design to give the building flexible work spaces and natural lighting. They also plan to add green concept elements (see “Going Green”) to obtain certification from the U.S. Green Building Council’s Leadership in Energy and Environmental Design.

The Río Piedras Campus’ research standing has greatly advanced in recent years. “Since the 1980s, we have doubled external funding every five years, and NCRR has played a significant role in that growth,” Fernández noted. UPR also has received NCRR support through the Research Centers in Minority Institutions program, which builds research capacity at minority institutions, and the Institutional Development Award program, which fosters health-related research in areas where NIH support historically has been low.

The new Río Piedras facility will give UPR another major boost. “Visiting professors can come to the university to share and exchange ideas with students, and we can hire new faculty with expertise in the areas we want to pursue,” Fernández explained.

The new building also will be a boon to the pharmaceutical and biotech industries — two of the main economic drivers in Puerto Rico. “The new building will allow us to provide some joint activities,” Fernández said. “It will allow us to conduct translational research and develop applications that can be transferred to industry.”

Situated between the Río Piedras and Medical Sciences campuses, the new research building will facilitate interaction between basic and clinical researchers. Fernández added that “the building shows the university’s commitment to research and development and its understanding of the importance that research has for the population — especially research for diseases that affect the population of Puerto Rico and other underserved groups.”

BOOSTING BRAIN POWER

At the University of California, Los Angeles (UCLA), School of Medicine, new construction helped fill a niche in the field of neuroimaging. “There has been a lot of development in techniques for acquiring information about brain structure and function,” said UCLA neuroscientist Arthur Toga. “But the development of ways to process, analyze and interpret these data has lagged behind.” To address this critical need, the university built the Laboratory of Neuro Imaging (LONI).

The centerpiece of the facility is the Data Immersive Visualization Environment (DIVE), a room dominated by a 12-foot, 150-degree, floor-to-ceiling concave screen on which scientists can project real-time computer graphics, high-definition video, or prerecorded demonstrations or slides.

Visually “diving” inside data has been essential to investigators trying to understand the connections among different regions of the brain to build 3-D maps of brain architecture. Toga, who is also the director of LONI, explained that these data “become unwieldy unless you can show them on a 150-degree screen. Then you can see connections that could not otherwise be seen. People enter the DIVE, and right away you can see the light come on. It is really amazing.”



■ The first phase of construction of a new research building at the University of Puerto Rico, Río Piedras Campus, is scheduled for completion in December 2009. It will produce 12 laboratories for research in neuroscience, cancer and molecular studies.



■ The Data Immersive Visualization Environment (DIVE) is the centerpiece of the Laboratory of Neuro Imaging at the University of California, Los Angeles, School of Medicine. The DIVE features a 12-foot, 150-degree, floor-to-ceiling concave screen on which scientists can project real-time computer graphics, high-definition video, or prerecorded demonstrations or slides.

The 8,427-square-foot building that houses LONI, constructed with \$1.96 million from NCRR in 2000 and matching funds from the university and other sources, brings together neurobiologists, computer scientists, physicists, mathematicians and even graduates from UCLA's School of Design. Toga is an 11-year recipient of P41 grant funding from NCRR for a Biomedical Technology Research Center that makes LONI's brain-mapping developments available to other scientists.

To encourage collaboration and communication among researchers with such disparate backgrounds, the building features many open spaces and glass walls. Display screens in every room allow researchers to share information with each other from anywhere in the building.

Similarly, the building's many curved walls not only are aesthetically pleasing but also mirror the research conducted at LONI. "We deal with biology, and in biology, there aren't many right angles," Toga said. "Whenever we could, we incorporated curved surfaces to reflect the challenges we face in doing science."

Toga mentioned that the only downside of the building is that it already feels too small. "We have a huge waiting list of students and visiting professors who want to come here," he said. "We would like to expand it further."

RESOURCE REJUVENATION

Sometimes significantly expanding a resource is the best way to meet growing demand. NCRR funding helped the New York Structural Biology Center (NYSBC) in New York City, a facility essential to a large community of scientists in the region, expand its size and capabilities.

In 2002, 10 research institutions in New York established NYSBC to address a critical scientific need. New York has a large community of structural biology researchers, who require

large and expensive equipment, such as high-field magnets for nuclear magnetic resonance (NMR) spectrometers used to determine the atomic structures of molecules. "New York's institutions made a large investment in the scientists who specialize in NMR but did not have the latest-generation instruments that they required to conduct their research," explained Willa Appel, executive vice president and chief operating officer of NYSBC. "Given the cost of these instruments and the difficulties in finding suitable locations for them, it made sense for the institutions to pool their efforts and resources in a shared facility."

Today, NYSBC supports the work of more than 60 laboratories and houses the largest and most advanced cluster of high-field NMR instruments in the United States or Europe, including two machines with magnet field strengths of 900 megahertz — more than 12 times as powerful as any hospital machine. It also contains three cryoelectron microscopes, which allow researchers to visualize biological samples at extremely low temperatures in their native environments without using any stains or fixatives. NYSBC operates two synchrotron beamlines for X-ray crystallography at the nearby Brookhaven National Laboratory. "NYSBC has helped us retain researchers in the New York region and has attracted new investigators to New York," Appel said.

To house so many powerful instruments in one place, architects and builders had to be creative. For example, because NMR instruments are extremely sensitive to vibration, architects designed massive concrete columns, 30 feet high and 16 feet wide, on which to place them. The columns are anchored directly to the bedrock and separated from the building's floor, "so that if you walk right next to the column, your steps will not generate vibrations that could affect the measurements," Appel explained. This approach worked so well for the magnets that the cryoelectron microscopes also were placed on concrete

columns. Because these microscopes are sensitive to noise, the equipment rooms were soundproofed as well.

Although past NCRR construction grants did not require “green” building practices (see “Going Green” on page 8), Appel noted that care was taken to minimize damage to the environment while renovating and expanding NYSBC. The first phase of construction, for example, involved renovating a gymnasium built in the 1930s and preserving some of its original features, such as an Italian-style loggia at the entrance.

In two subsequent phases of construction, both supported in part by NCRR funding, the original building was extended by 12,000 square feet, and a new 9,500-square-foot building was constructed next to it. Appel asked the architects to adjust the location of the new building by a few feet to preserve a large Copper Beech tree on the site. “We went to great lengths to save that tree,” Appel said. “We had an arborist come and look after it during the construction. I am happy to say that the tree is thriving.”

INVESTMENTS IN INSTRUMENTATION

Buildings are critical to bringing scientists together, but science cannot happen without the right equipment. NCRR’s High-End Instrumentation (HEI) and Shared Instrumentation Grant (SIG) programs help researchers obtain these vital resources.

The Longwood Small Animal Imaging Facility (LSAIF), which opened at the Beth Israel Deaconess Medical Center of Harvard Medical School in July 2008, owes its existence in part to an HEI grant. With more than \$900,000 from NCRR, LSAIF obtained two state-of-the-art imaging systems with exquisitely high sensitivity. Harvard then provided another \$1.4 million to help establish the facility. “We could not have afforded to do this without NCRR support,” said John V. Frangioni, co-director of LSAIF.

LSAIF provides Harvard researchers access to techniques for obtaining images of the internal organs and body structures of small animals, including positron emission tomography, single positron emission computed tomography and computed tomography imaging. Because these techniques — and similar instruments — also are used to examine people, the results of studies conducted at LSAIF can be translated easily to humans.

In one such study, researchers used the facility’s imaging systems to develop a new diagnostic agent for detecting tiny calcium deposits, or microcalcifications, in breast tissue. These deposits are associated with increased cellular activity, which is not usually malignant; however, tight clusters of microcalcifications sometimes indicate early breast cancer.

The current method for detecting microcalcifications in the breast, mammography, is relatively insensitive and nonspecific.

ARRA AWARDS

NCRR construction and instrumentation grants are just two types of grants administered under ARRA. Below are NCRR-supported programs as well as NIH-wide ARRA grant programs in which NCRR is participating.

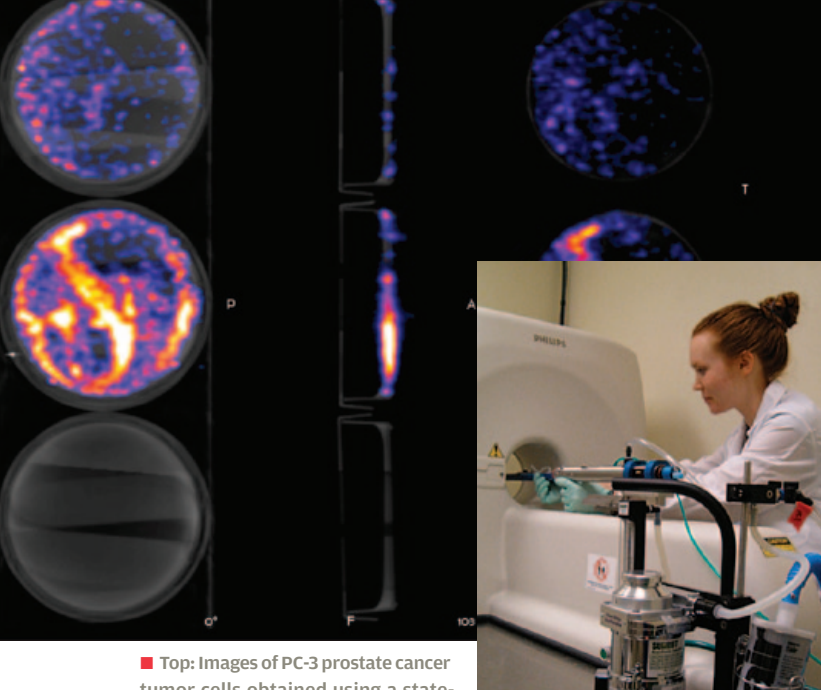
NCRR-supported Programs

- **Administrative Supplements for NCRR Awards** to accelerate the tempo of scientific research on active grants.
- **Competitive Revision Applications** to leverage the resources, expertise and infrastructure of the NCRR centers and center-like programs through significant expansion of the scope or research protocol of approved and funded projects.
- **Core Facility Renovation, Repair and Improvement (G20)** to upgrade extramural core facilities that support biomedical and behavioral researchers. The maximum award is \$10 million.
- **Extramural Research Facilities Improvement Program (C06)** to support construction, renovation or repair of extramural biomedical or behavioral research facilities. The maximum award is \$15 million.
- **High-End Instrumentation (S10)** to purchase a single major item of equipment to be used for biomedical research that costs at least \$600,000. The maximum award is \$8 million.
- **National Networking and Resource Discovery (U24)** to develop, enhance or extend infrastructure for connecting people and resources to facilitate discovery of individuals and resources by scientists and students and encourage interdisciplinary collaboration and scientific exchange.
- **Shared Instrumentation (S10)** to purchase shared instruments costing between \$100,000 and \$500,000.

NIH-wide Programs

- **Academic Research Enhancement Award (R15)** to stimulate research in educational institutions that provide baccalaureate or advanced degrees for a significant number of the nation’s research scientists but have not been major recipients of NIH support.
- **Administrative Supplements Providing Summer Research Experiences for Students and Science Educators** to encourage students to pursue research careers in the health-related sciences and to provide elementary, middle and high school teachers; community college faculty; and faculty from non-research-intensive institutions with short-term research experiences in NIH-funded laboratories.
- **Biomedical Research, Development and Growth to Spur the Acceleration of New Technologies (BRDG-SPAN) Pilot Program (RC3)** to accelerate the transition of research innovations and technologies toward the development of products or services that will improve human health, help advance the mission of NIH, and create significant value and economic stimulus.
- **NIH Challenge Grants in Health and Science Research (RC1)** to support research on topic areas that address specific scientific and health research challenges in biomedical and behavioral research that would benefit from significant two-year jump-start funds.
- **Small Business Catalyst Awards for Accelerating Innovative Research (R43)** to encourage small businesses that propose to accelerate innovation through high-risk, high-reward research and development that has commercial potential and is relevant to the mission of NIH.

For additional information about NCRR’s programs funded through ARRA, visit www.ncrr.nih.gov/recovery. Other information about ARRA can be found at www.nih.gov/recovery and www.hhs.gov/recovery.



■ Top: Images of PC-3 prostate cancer tumor cells obtained using a state-of-the-art SPECT/CT imaging system purchased through NCRR's High-End Instrumentation program. Right: Research assistant Elaine P. Lunsford conducts an experiment using the SPECT/CT system at the Longwood Small Animal Imaging Facility at the Beth Israel Deaconess Medical Center of Harvard Medical School.

For example, mammography cannot chemically distinguish between benign and malignant deposits. However, the new procedure and agent developed by Frangioni's group can do just that, at least in rodents. "This study is a great example of how the instrument let us do something that we could never, ever have done otherwise," Frangioni said.

Other researchers are using the imaging instruments at LSAIF to develop animal models for studying prostate cancer, and still others are designing methods to detect brown fat and study how it forms, which may lead to new ways to treat obesity. "The facility completely relieves the investigator of any worries," Frangioni explained.

ACCELERATING RESEARCH POWER

The SIG program provides funding for NIH-supported investigators to obtain or update instruments too expensive to be purchased through research program grants. David Serreze, an investigator at the Jackson Laboratory in Bar Harbor, Maine, received a SIG award to purchase an analytical cytometer for the laboratory's Flow Cytometry Service. The instrument allows researchers to identify and characterize various subpopulations of cells. With the ability to detect up to 13 colors emitted by laser excitation of labeled antibodies that bind in various combinations to particular cell types, it is "top of the line when it comes to cytometry," Serreze said.

The instrument allows researchers to examine many more characteristics in a single sample of cells than they could with instruments that detect fewer colors. For example, dyes can be

applied to a sample to label up to 13 distinct protein markers on the cells' surfaces. The advantage of this technique is evident from Serreze's work. Using mouse models of type 1 diabetes, an autoimmune disease in which immune cells destroy the cells of the pancreas, Serreze has characterized the types of immune cells present in the pancreas to gain insight into the disease. "We typically don't have large samples of cells, and the new cytometer has been invaluable for getting as much information as possible out of those samples," he explained.

Serreze's lab is only one of 11 labs that have used the cytometer in its first year of service. The instrument is helping scientists working on topics that range from stem cells to lymphoma. "It benefited far more people than I ever imagined," Serreze said.

The Jackson Laboratory, which is housed in several facilities built with NCRR C06 construction funds, has made many contributions to mouse genetics research and the development of mouse models for human disease. Mouse strains developed by scientists at the laboratory are made available to the entire scientific community. "It is a value-added component for the mouse user community as a whole," Serreze said. "If we characterize mice better, that will help others. A scientist may have never thought of using mouse x for looking at a particular disease. Maybe they will think of using that mouse because of some added characteristics we have provided."

From a research building in Puerto Rico, to a neuroimaging center at UCLA, to state-of-the-art equipment at The Jackson Laboratory, NCRR-supported resources and facilities not only stimulate advancements in health research, they also stimulate economic growth in the scientific arena as well as in many other sectors. As ARRA-funded grants continue to make their way into the biomedical research community, they will give rise to brand new facilities, better-equipped research laboratories, multidisciplinary training programs for young scientists and clinicians, cutting-edge projects, and countless other examples of the far-reaching impact of investing in science. ■

GOING GREEN

The construction grants awarded through ARRA encourage grantees to implement several elements of sustainable design in funded facilities. These elements ensure energy efficiency, reduce the environmental impact of building materials and minimize the use of compounds that deplete the ozone. All improvements and repair projects that cost \$10 million or more or affect 40 percent or more of the overall floor area in a building must obtain certification from the U.S. Green Building Council's Leadership in Energy and Environmental Design or the Green Building Initiative's Green Globes System Certification rating system.

Filling the Vital Need for Veterinary Researchers

HIN1 flu. SARS. Ebola. Each of these feared viral outbreaks came from animals. Each uncovered a critical shortage of veterinarians conducting cutting-edge research.

“Veterinarians are in a position to take the lead in coming up with improved diagnostics, working out better treatments and finding ways to prevent disease spread,” said Kent Lloyd, associate dean for research and graduate education programs at the University of California (UC), Davis.

Michael Atchison, a professor of biochemistry at the University of Pennsylvania, agreed. “Veterinarians receive broad comparative medicine training,” he said. “This brings something special to science. They think a little differently. They know the right questions.”

Lloyd and Atchison are principal investigators on NCRR veterinary training grants — one of several ways NCRR encourages and supports veterinary students in research. Other organizations also have begun to recognize the need for more of these researchers. In the past five years, the National Research Council released two reports on the pressing need for veterinary researchers, who could improve both animal and human health.

“Translational research has a great need for veterinary scientists, but not enough veterinarians go into research,” said Franziska B. Grieder, director of the Division of Comparative Medicine at NCRR. “This is primarily a cultural problem. Most veterinary students aren’t aware of research career opportunities.”

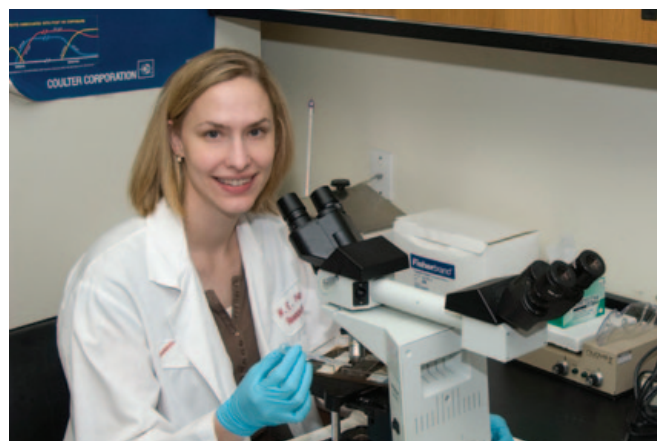
To address this challenge, NCRR attempts to engage veterinary students early by offering summer research experiences after the first or second year of veterinary school. NCRR awards a T35 short-term training grant to about a dozen institutions for students to conduct research in various laboratories.

Students who discover an affinity for research through their summer T35 projects can apply to renew their funding. Penn alumna Katherine Hammerman took advantage of this opportunity. “I used the summer research grant to get my feet wet in the research programs at Penn and to see if I was willing and able to commit to a lengthy V.M.D.–Ph.D. joint program,” she said. Her research focused on germ-cell biology, using mice as a model for humans. “It was a very positive experience.”

Hammerman, who also worked in a laboratory as an undergraduate, said that interactions with colleagues who had earned or were working toward research degrees helped convince her to do the same. She finished her V.M.D. in 2002 and received her Ph.D. in 2006. Following her dissertation work, which centered on the cell biology of the parasite *Toxoplasma gondii*, she has continued to work in infectious diseases through a postdoctoral fellowship at the NCRR-supported New England Primate Research Center. Her career trajectory is not unusual for Penn students who participate in the T35 program. Though most continue their veterinary training with the intention of working in animal clinics, nearly half each year get hooked on research and go on to postgraduate education.

For nearly two decades, Penn has offered its program to about 20 students per summer. Over the years, Atchison, who serves as the principal investigator of one of Penn’s T35 grants, has collected data on these students’ careers. Those who have completed T35 training are about twice as likely as their peers to go on to further education. Eight times as many go into a research degree program, just as Hammerman did.

For veterinary students interested in research but not ready to commit to earning a Ph.D., NCRR’s predoctoral T32 program supports a year of research in a biomedical laboratory. The



■ Katherine Hammerman, an NCRR-supported T32 postdoctoral fellow, investigates simian immunodeficiency virus expression in nonhuman primates at the New England Primate Research Center. She previously received NCRR support through two T35 summer training grants at the University of Pennsylvania.



■ Brian Bird wears a containment suit to study viral hemorrhagic fevers in a Biosafety Level 4 laboratory. His research, conducted at the Centers for Disease Control and Prevention while he was a graduate student at the University of California, Davis, was supported by NCRR T32 and T35 grants.

research year can lead directly to dissertation research or simply become a pause in a student's veterinary studies. Between predoctoral T32s and T35s, NCRR funds about 150 veterinary students every year.

Lloyd directs a long-standing summer T35 program as well as a predoctoral T32 program at UC Davis. Students have noted in exit interviews that they appreciated the opportunity to pursue something they were curious about and gain experience in a variety of subjects. "This enabled them to decide whether to move on to a more formal training program," Lloyd said.

Thus far, all of the UC Davis predoctoral T32 students have gone on to pursue research degrees. One of them was Brian Bird, who noted that "there is no traditional career track (for veterinarians in research). It is hard to have a defined role model." However, his experience in graduate school gave him just that. He conducted research at the Centers for Disease Control and Prevention (CDC), where he studied viral hemorrhagic fevers. This group of diseases includes Ebola, hantavirus and Rift Valley fever and requires the highest level of containment precautions. Only four laboratories in the country can conduct such research.

Part of Bird's dissertation research involved developing a candidate vaccine for Rift Valley fever, a disease that primarily affects livestock but can also cause epidemics in people. Bird finished his Ph.D. last year and his V.M.D. this year. He is now returning to the CDC laboratory as a research scientist. He expects his first graduate student trainee to come from UC Davis this year.

Most UC Davis students who pursue dual degrees in veterinary medicine and research stay on campus because of the large selection of mentors, Lloyd said. Students can work in laboratories anywhere on campus, such as NCRR-funded primate or mouse centers or the NCRR-funded Clinical and Translational

Science Center. UC Davis also offers a postdoctoral T32 grant option to complement the predoctoral program, so the funding opportunities for students can continue.

Postdoctoral T32s pay veterinarians' stipends for up to three years of research (see "Bringing Veterinarians into Biomedical Research," *NCRR Reporter*, Spring 2005). NCRR funds approximately 80 veterinarians in various levels of training every year through postdoctoral T32s. Hammerman receives funding through the program while working at the New England Primate Research Center.

She has plans for her next step in research funding: to apply for a K01. The K01 funding mechanism, also known as the Special Emphasis Research Career Award (SERCA) in Pathology and Comparative Medicine, supports veterinary researchers as they transition toward independent research. The award currently supports 25 veterinarians, including salary and up to \$20,000 in research support.

Ian Davis, an assistant professor of veterinary biosciences at The Ohio State University, had a K01 grant for five years to support his postdoctoral fellowship at the University of Alabama at Birmingham. He studied viral infections of the lung, using mice as models for humans. "The SERCA is a great opportunity," he said. "It helped me get my foot in the door as a research-track faculty member."

After his third year of K01 funding, Davis moved to his current tenure-track position. "I would not be an independent researcher without SERCA," he reflected. "I could not possibly have achieved a faculty position. Ohio State wanted a veterinarian actively involved in basic biomedical research and able to attract NIH-level funding." Since arriving at Ohio State, he has won grants from the American Heart Association and the National Institute of Allergy and Infectious Diseases. He continues to work on lung biology in mice, conducting studies on the influenza virus and fluid buildup.

Davis added, "When you're working on influenza, you feel that you could make a big difference for a lot of people, and maybe a lot of animals, too." That is a hope that NCRR's Grieder shares. Getting more veterinarians involved in research should ease the difficult transition from the bench to the clinic, and NCRR is playing a leading role in training and supporting those veterinarians. "It is a very powerful program," Grieder said. "It fills an important niche in biomedical research — specifically, translational science. But most of all, it is training a new generation of veterinary researchers to be partners on translational research teams."

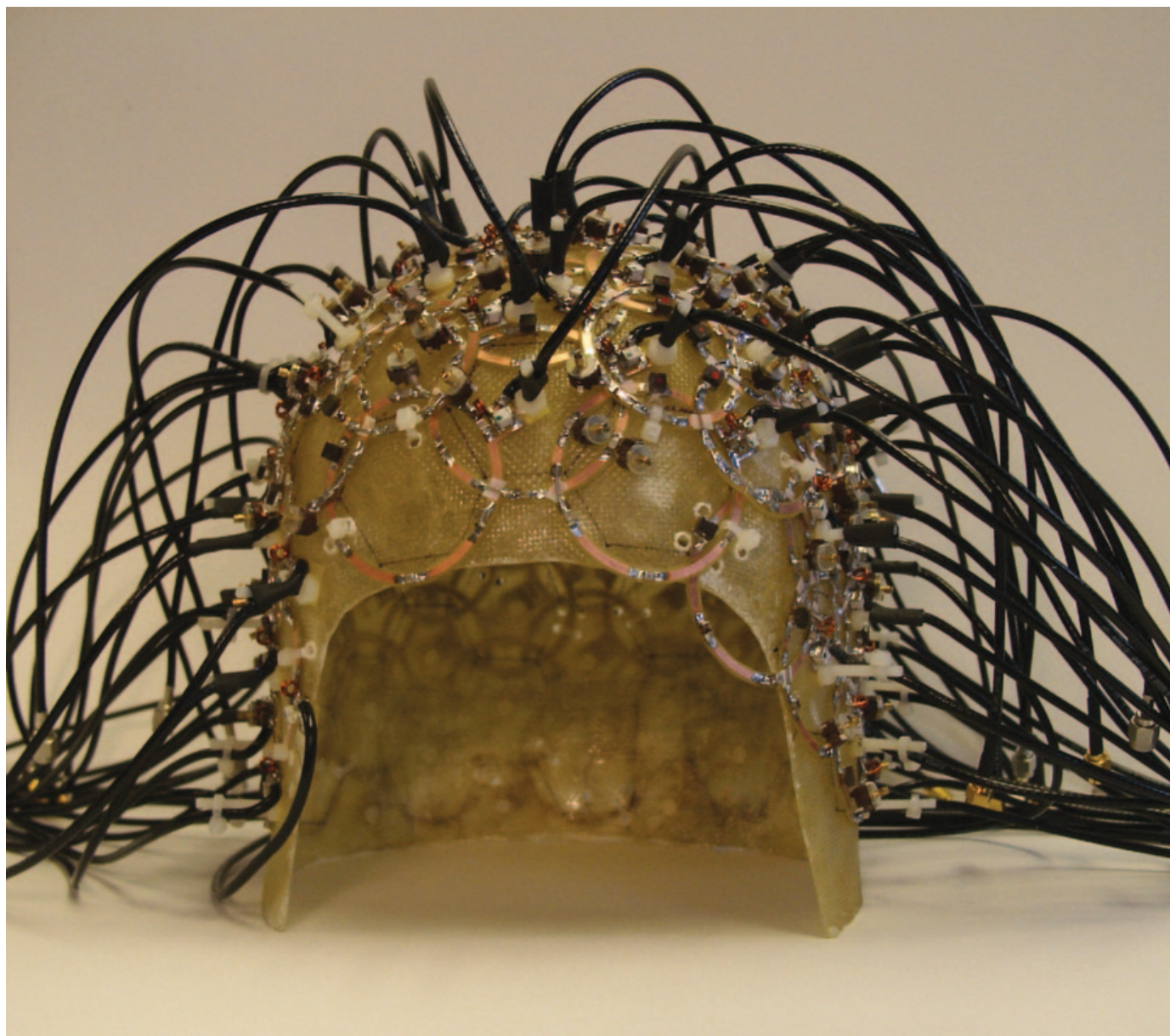
—LILA GUTERMAN

Examining the Brain's Fine Structure

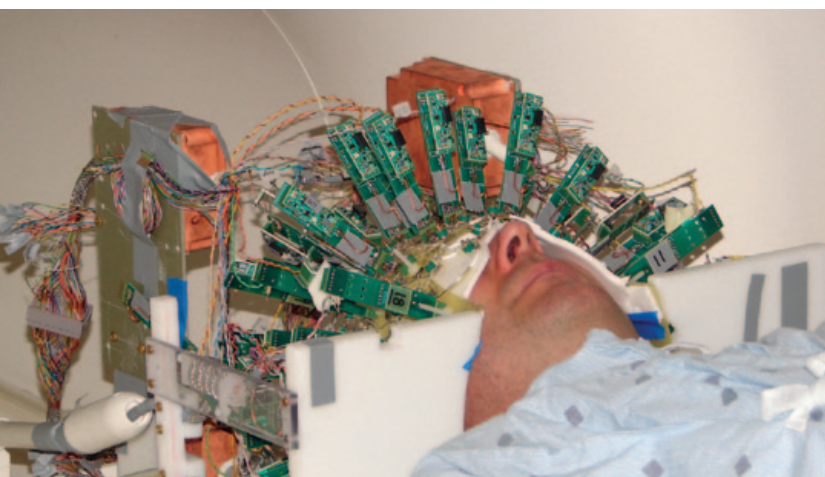
Few experiences at the doctor's office cause more frustration than hearing "we've completed all the tests, but we still don't know what's causing your disorder." For a person with epilepsy, the frustration is understandable. If doctors can find a lesion in the patient's brain, surgeons might be able to remove it, offering the possibility of full recovery.

But if nothing abnormal shows up on the brain scans, the patient is left to suffer seizures and follow drug regimens that are sometimes ineffective and produce unwanted side effects.

Now these patients have new hope, thanks to research at the Center for Functional Imaging Technologies at Massachusetts General Hospital (MGH), an NCRR-supported Biomedical



■ A prototype helmet bears 90 overlapping coils that pick up an MRI signal. The helmet, designed by NCRR-supported researchers at Massachusetts General Hospital, defied scientific dogma to make more powerful brain scans possible.



■ A subject wearing the experimental multi-coil helmet is ready to slide into the MRI magnet. Green preamplifiers radiate from each MRI signal detector on the helmet. The preamplifiers magnify the detected electronic signals and send them to a digitizer and a computer, which reconstructs and combines the data to form the final high-resolution image of the subject's brain.

Technology Research Center (BTRC). These researchers have created an MRI brain-scanning instrument so powerful that it can pick up the tiniest of lesions, even those as small as a blood vessel. The instrument uses dozens of overlapping coils that pick up the MRI signal, all built into a helmet that fits closely to the patient's head.

The Center for Functional Imaging Technologies is one of more than 50 NCRR-funded BTRCs across the United States that enable researchers to develop and distribute new technologies and methodologies. At MGH, the center allowed researchers to realize a clinically important technique and make a discovery that challenged scientific norms.

"The thought was that it wouldn't really work," said Bruce R. Rosen, principal investigator of the center. Previously, scientists thought that small coils could provide images only of tissue near the coil, not deep within an organ like the brain. NCRR funding enabled the researchers to build prototype coils and purchase high-field magnets to test their idea. The result? "The established dogma wasn't right," Rosen said. Instead, the coils worked together to produce high-resolution images throughout the brain.

The image resolution was more than double that of images obtained using standard techniques. Such a jump would previously have required doubling the strength of the magnet, a multimillion-dollar expense. Rosen added that the multi-coil helmet allows much faster imaging of the brain at a fraction of the cost.

When the researchers combined the helmet with a higher-power magnet, the two technologies aligned surprisingly well.

"They're made for each other," Rosen said. Resolution increased nearly 10-fold in some parts of the brain. NCRR also supported the MGH team's development of the computational tools to analyze data from the scans.

The MGH team published its results on a 32-coil design in the journal *Magnetic Resonance in Medicine* in 2006. A manuscript about a 96-coil design was published in July 2009 in the same journal.

Already, the technology company Siemens has collaborated with MGH to commercialize a helmet based on the new design, using 32 coils and a 3-Tesla magnet. Meanwhile, the researchers have pushed their design to 128 coils and used it with more powerful magnets. The MGH team's experimental helmet looks a bit like medieval armor with wires attached, whereas the commercial version of the helmet looks like something a stormtrooper might wear in *Star Wars*.

"We are seeing things we just weren't able to see before — things like very small brain tumors or lesions that cause epileptic seizures," Rosen said.

The move from experimental technology to commercialized product has been rapid, and Rosen envisions continued progress in providing patients with access to the new scanners. "I would guess that in the not-too-distant future, these will become ubiquitous," he said.

"They're making a major step to move high-resolution imaging to the clinic for diagnostics and treatment," said Abraham Levy of NCRR's Division of Biomedical Technology. "You can use the MGH technology to study schizophrenia, Alzheimer's disease and all kinds of other disorders that relate to the brain." With NCRR support, Rosen and his colleagues continue to investigate the optimal number of coils. They also hope to develop a multi-coil instrument to use with children. Because children are unable to hold still for very long, they often have to undergo anesthesia to get an MRI scan. If the extra coils can make the scanning process faster, they might enable MRI without anesthesia even for small children.

For a doctor or technician, administering an MRI using the coil-encrusted helmet is not that different from providing a traditional MRI scan of the brain: both involve placing a head wrap on the patient and then sliding him or her into a large, doughnut-shaped magnet.

"The patient experience is essentially identical to the way it was before," Rosen said. "However, now there is a stronger potential for a diagnosis that can lead to a more effective treatment and, ideally, a long-lasting, life-altering impact." ■

—LILA GUTERMAN

Expanding Drug Discovery in Kansas

Building on expertise from its school of pharmacy, the University of Kansas established the Center for Cancer Experimental Therapeutics (CCET) in 2000. The center is one of 83 NCRR-funded Centers of Biomedical Research Excellence (COBRE). “CCET researchers search for new drug leads and delivery methods for therapeutic agents for various forms of cancer,” said Barbara Timmermann, CCET’s principal investigator.

Two consecutive, five-year, \$10 million grants from NCRR allowed CCET to launch a medicinal chemistry core with state-of-the-art facilities for synthesizing chemical compounds as well as a high-throughput screening core for identifying compounds that act in particular disease pathways. The screening core uses specialized equipment to screen entire “libraries” of candidate compounds. Such facilities are standard components of drug development programs at biotech and pharmaceutical companies.

Timmermann said having this infrastructure in place helped the university secure an \$8.1 million grant from the Ewing Marion Kauffman Foundation in 2008. The grant established the Institute for Advancing Medical Innovation (IAMI), which builds on existing resources to speed the translation of medical innovations from the lab to patients.

“This is an excellent example of how COBRE funding works,” said Sidney McNairy, director of NCRR’s Division of Research Infrastructure. “It lays the groundwork to establish a research platform in a specific area, which in turn enables the

university to better compete for additional research funding and attract leading researchers.”

CCET scientists already are using advanced methods in medicinal chemistry and high-throughput screening for cancer research and drug discovery — the kinds of projects IAMI will support. “CCET’s medicinal chemistry core will be particularly important to IAMI because the core is recognized as one of the top programs in the country,” Timmermann added.

The timing for establishing IAMI could not have been better. Drug development has traditionally been the domain of the pharmaceutical industry, but now small biotech companies and universities are taking leading roles.

Among the promising molecules developed at the University of Kansas is a compound that blocks heat shock protein 90 (Hsp90), a key protein that helps cells grow. Brian Blagg, working at another COBRE on protein structure and function at the university’s Lawrence campus, led the initial work to develop an Hsp90 inhibitor, which prevents cancer cells from continually dividing and multiplying.

“Companies are producing a number of Hsp90 inhibitors, but many have side effects,” said Sitta Sittampalam, director of drug discovery and lead generation at IAMI. “We have discovered several compounds that target a different region of Hsp90 than other drugs and as a result they seem to have fewer side effects.”

IAMI’s mission is to make new compounds like these and new medical devices available to patients more quickly. The institute will provide seed funds for several new projects each year, encouraging sharing of resources within the university as well as partnerships with other institutes and industry.

IAMI has already attracted additional funding to the university. “It all started with NCRR funding 10 years ago,” said Joan Hunt, vice chancellor for biomedical research infrastructure at the University of Kansas Medical Center. “We are now moving forward in carving out a place in translational research.” ■

—LAURA BONETTA



■ Barbara Timmermann, who leads the NCRR-funded Center for Cancer Experimental Therapeutics, and Sitta Sittampalam, director of drug discovery at the Institute for Advancing Medical Innovation, develop new cancer drugs and therapies at the University of Kansas.

TO GAIN ACCESS: NCRR’s COBRE are part of the Institutional Development Award (IDeA) program, which fosters health-related research and enhances the competitiveness of investigators at institutions in states in which the success rate for applications to NIH has historically been low. The program also serves unique populations, such as rural and medically underserved communities. For more information, visit www.ncrr.nih.gov/idea.

Dynamic Cells at the Maryland Science Center

Imagine walking through a two-story human cell with semi-transparent teal walls, mitochondria the size of eight-foot-high water balloons and the whooshing sound of blood traveling through gigantic arteries. Visualize modern dancers interpreting cell processes and encouraging you to do the same. You've just come close to the experience of visiting the Maryland Science Center's newest permanent exhibit, "Cells: The Universe Inside Us."

In March 2009, after four years of development, the museum opened this interactive, 4,000-square-foot exhibit that explores the microscopic world of human cells, thanks to a \$1.3 million NCRR Science Education Partnership Award (SEPA).

Designed for students in grades 5 through 12 as well as adult visitors, "Cells" uses hands-on, experiential activities to explain cell biology. In turn, visitors can gain an appreciation of the impact of basic and clinical research on their lives and explore possible careers in health professions, including biomedical research. High-school student Chasidy Chambers summed

up the experience for many students: "When you see it visually, it gives you a better understanding."

Making science exciting and inspiring for young people was a driving force for the exhibit's developers as they worked closely with local artists, multimedia specialists, graphic designers and students. They also collaborated with renowned scientific advisors from Johns Hopkins University, the University of Maryland and the NCRR-supported National Center for Microscopy and Imaging Research at the University of California, San Diego, to ensure the accuracy and quality of the science presented. In all, more than 100 professionals helped create the exhibit.

The result? Dozens of multi-sensory learning experiences. Students and others learn about the potential stem cells hold for replacing cells and tissues that have been lost to injury or disease. Modern dancers encourage participants to explore the impact of their own movement at the cellular level. Visitors can tap a reflective screen to see how their own muscle, heart and brain cells behave. Plexiglas arteries demonstrate the difference between free-flowing red blood cells and fatty buildup. "The whole is bigger than the sum of its parts," said graphic artist Jeanne Krohn as she shifted magnets on the wall of words she helped design to inspire scientific inquiry.

With an estimated 500,000 or more visitors every year, "Cells" is expected to have wide exposure and appeal. Another major funding partner, the MetLife Foundation, has agreed to develop a traveling companion exhibit that will bring the same experience to students all over the country.

Tony Beck, NCRR's SEPA program officer, is hopeful that this exhibit and others funded by SEPA grants will expose the public to the wide arc of NIH-funded research and how it affects their lives. "SEPA projects at science centers and museums provide an interactive environment in which the community can learn about science and understand the relationship between one's lifestyle and one's health," he said. ■

—LAURA BONETTA AND REBECCA RAZAVI



■ A new NCRR-funded exhibit at the Maryland Science Center in Baltimore explores the world of human cells. Here, a visitor examines a model of the DNA double helix. Each person's body contains trillions of cells, all of which have essentially the same DNA.

TO GAIN ACCESS: NCRR's SEPA program funds innovative science education projects. Such projects create partnerships among biomedical and clinical researchers and K–12 teachers and schools, museums and science centers, media experts, and other educational organizations. For a list of currently funded projects, please visit the SEPA Web site at www.ncrrsepa.org/proj_active.jsp.

Highlights From Recent National Meetings

Collaborations among researchers and institutions nationwide are improving access to care, maximizing the use of critical resources and speeding scientific discoveries. Many of NCRR's programs establish and encourage such collaborations in an effort to translate laboratory findings into better treatments for patients. With this goal in mind, NCRR jointly sponsored four summer meetings to explore programs that are advancing science and medicine through shared expertise and resources. Archived videocasts and meeting materials are available at www.ncrr.nih.gov/news_&_events/#past_events.

CLINICAL RESEARCH MANAGEMENT

In June, leaders of the Clinical and Translational Science Award (CTSA) consortium met to create a plan to improve clinical research management at CTSA sites nationwide. The **Second Annual Clinical Research Management Workshop** was hosted by the Yale Center for Clinical Investigation and supported by an NCRR-funded conference grant. The workshop brought together more than 60 academic medical centers, including 38 CTSA's; NIH; industry; and other organizations to discuss ways to develop evidence for improved efficiency in clinical research management. These discussions led to a plan that recommends 1) using data-driven methods of process improvement, 2) motivating "champions of change" at each site to drive improved processing efficiency, 3) publishing comparable data on each site to document the effects of process changes,

4) sharing best practices as teaching tools, 5) adopting standards in clinical research management across the CTSA consortium, and 6) monitoring data periodically.

THE FUTURE OF TELEHEALTH

Representatives from federal agencies, universities and the high-tech industry attended the **Future of Telehealth: Essential Tools and Technologies for Clinical Research and Care** conference in late June to discuss the latest advances and recommend directions for developing and using telehealth technologies. Progress has ranged from harnessing the explosion of Web-based digital devices among consumers for personalized health care to facilitating research and health care among underserved populations through telehealth technology. Studies and applications described at the conference have demonstrated how implementing telehealth technologies could improve preventive medicine, health care education, health care access by the medically underserved, collaborative clinical and translational research, and public health systems. In light of these benefits, participants recommended that NIH facilitate collaboration and multi-center telehealth research and development, promote telehealth use among health care professionals, develop translational research software, and explore ways to enhance information security.

EFFICIENT CORE FACILITIES

In July, NCRR and the NIH Office of Extramural Research convened the **Efficient Management and Utilization of Core Facilities** workshop. Core facilities offer centralized, shared resources,

such as instrumentation and other technology; support for cellular, animal or human studies; and expert consultation. These resources often are difficult for researchers to find or afford on their own and present a myriad of management challenges. The workshop convened more than 400 participants, including core administrators, government officials, researchers and other stakeholders, to discuss the state of NIH-funded core facilities and strategies for maximizing their use and efficiency. Suggestions included consolidating core facilities at the institutional and regional levels, enhancing networking among researchers and cores, and establishing a national registry. The workshop organizers will use the information and feedback provided to more effectively and efficiently support needed resources.

RARE DISEASES RESEARCH

NCRR and the NIH Office of Rare Diseases Research held a conference in mid-July that brought together investigators, coordinators, patient advocacy groups and government leaders to discuss the challenges and opportunities of studying rare diseases. The **Advancing Rare Diseases Research Through Networks and Collaboration** conference showcased some of the successes and lessons learned from the Rare Diseases Clinical Research Network. This collaborative network of multiple research consortia, each focusing on a subset of rare diseases, conducts studies to discover disease mechanisms, develop diagnostics, identify biomarkers and test new treatments. It also trains new investigators in rare diseases research. Strategies for forming effective teams,

sharing best practices, advancing basic research to clinical testing and disseminating research results into practice were discussed as part of interactive conference panels. Many speakers noted that collaboration across disciplines, across geographic regions and among partners is critical to advancing research.

NCRR continues to encourage collaborations to advance science and medicine and ultimately improve patient care.

NCRR Announces New Advisory Council Members

NCRR has selected four new members to serve on its National Advisory Research Resources Council. Council members advise NCRR on its policies and programs, and review grant applications. The new council members, listed below, are leaders in their fields and will serve four-year terms.

Mark O. Lively is a professor of biochemistry at Wake Forest University School of Medicine. Since 1983, he has directed the protein and DNA chemistry laboratories in the Biomolecular Resource Facility of the university's Comprehensive Cancer Center, providing support and expertise to many NIH-funded research projects. Lively is the 2009–2010 president of the Federation of American Societies



for Experimental Biology and is past president of the Association of Biomolecular Resource Facilities. An active peer reviewer of NCRR grant programs, he is currently analyzing the structure of proteins involved in iron transport and regulation of high blood pressure. He also has developed a test to determine if

an individual has gastroesophageal reflux or acid reflux disease.

Joel R. Stiles is the director of the National Resource for Biomedical Supercomputing (NRBSC) at the Pittsburgh Supercomputing Center. He is an associate professor in the Department



of Biological Sciences and the Lane Center for Computational Biology at Carnegie Mellon University, and he holds faculty appointments in the Departments of Neuroscience and Computational Biology at the University of Pittsburgh. His research focuses on the microphysiology of cells and synapses — tiny gaps between nerve endings — and how these microscopic building blocks act in the body and contribute to neuromuscular disease. Stiles is a co-developer of *MCell*, a Monte Carlo simulator of cellular microphysiology, and the principal architect of *DReAMM* (Design, Render, and Animate *MCell* Models). He directs the Computational Modules in Science Teaching program and other educational outreach activities at NRBSC.

David S. Weir directs the Office of Economic Innovation and Partnerships at the University of Delaware. Over a 40-year career, he has held leadership positions in both private and academic sectors. Weir lectured at the University of St. Andrews in Scotland before joining the DuPont Co. in Wilmington, Del. As vice president for global research and development in the agriculture segment, he played a key role in developing DuPont's worldwide capability in agriculture, plant science and biotechnology.



Before retiring, he participated in the planning initiative to shift DuPont's focus from polymers and fibers to life sciences. After retiring, Weir became director of Grupo Vicunha in Brazil, and in 1998, he became founding director of the Delaware Biotechnology Institute. He accepted his current position in 2008 as part of a new initiative to increase recognition of the University of Delaware as a center of invention, innovation and entrepreneurship and a contributor to economic development in the state and region.

M. Christine Zink is a professor and director of the Department of Molecular and Comparative Pathobiology at Johns Hopkins School of Medicine. Zink is a veterinary pathologist with expertise in the causes of infectious diseases. She



developed the premier animal model of HIV-associated neurological disease and used it to show that the antibiotic minocycline prevents HIV replication and HIV-associated neurological disease. These studies helped initiate ongoing clinical trials in the United States and Africa. Zink leads training programs in veterinary pathology and laboratory animal medicine and is director of admissions for the Cellular and Molecular Medicine Graduate Program at Hopkins. She is on the board of directors for the American Association of Veterinary Medical Colleges and was named 2009's Outstanding Woman Veterinarian of the Year by the Association of Women Veterinarians Foundation. ■

For a complete list of current council members, visit www.ncrr.nih.gov/about_us/advisory_council/roster.asp.